#9

Atty. Docket No.: 25436/1652 PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Davis, et al.	Examiner:	Not yet assigned
Serial No.:	10/021,818		
Filed:	December 13, 2001	Group Art Unit:	1651
Entitled:	"Dimeric Fluorescent Polypeptides"		
		Conf. No.:	5874

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8a

I hereby certify that this correspondence (and any paper or fee referred to as being enclosed) is being deposited with the United States Post Office as First Class Mail on the date indicated below in an envelope addressed to: U.S. Patent and Trademark Office, Box: Sequence, P.O. Box 2327, Arlington, VA 22202.

Kathleen Williams
Name of Person Mailing Paper

Signature of Person Mailing Paper

U.S. Patent and Trademark Office
Box: Sequence
P.O. Box: 2327
Arlington, VA 22202

AMENDMENT AND RESPONSE TO NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Sir:

This is filed in response to the Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures mailed in the above-noted U.S. patent application on May 29, 2002. Kindly enter the following amendments and remarks.

In the Specification:

- On page 6, replace the paragraph at lines 8-15 with the following replacement paragraph:

In one embodiment, the first polypeptide and the second polypeptide encoded by the polynucleotide are peptide bonded to each other via a linker sequence. In a preferred embodiment, the linker sequence encoded by the polynucleotide is from 5 to 50 amino acids long. In a further preferred embodiment, the linker sequence comprises one or more iterations of a peptide, for example the peptide RARDPRVPVAT (SEQ ID NO: 8; i.e., Arg-Ala-Arg-Asp-Pro-Arg-Val-Pro-Val-Ala-Thr). In a further preferred embodiment, the linker sequence is

selected from the group consisting of (Arg-Ala-Arg-Asp-Pro-Arg-Val-Pro-Val-Ala-Thr)$_n$ (SEQ ID NO: 8), (Gly-Ser)$_n$, (Thr-Ser-Pro)$_n$, (Gly-Gly-Gly)$_n$, and (Glu-Lys)$_n$, wherein n is 1 to 15.

- On page 15, replace the paragraph at lines 3-14 with the following replacement paragraph:

As used herein, the term "linker sequence" refers to a sequence of peptide bonded amino acids that joins or links by peptide bonds two amino acid sequences or polypeptide domains that are not joined by peptide bonds in nature. A linker sequence is encoded in frame on a polynucleotide between the sequences encoding the two polypeptide domains joined by the linker. A linker is preferably 5 to 50 amino acids in length, more preferably 10 to 20 amino acids in length. An example of linkers useful in the invention are the Gly-Ala linkers taught by Huston et al., U.S. Patent No. 5,258,498, incorporated herein by reference. Additional useful linkers include, but are not limited to (Arg-Ala-Arg-Asp-Pro-Arg-Val-Pro-Val-Ala-Thr)$_{1-5}$ (SEQ ID NO: 8; Xu et al., 1999, Proc. Natl. Acad. Sci. U.S.A. 96: 151-156), (Gly-Ser)$_n$ (Shao et al., 2000, Bioconjug. Chem. 11: 822-826), (Thr-Ser-Pro)$_n$ (Kroon et al., 2000, Eur. J. Biochem. 267: 6740-6752), (Gly-Gly-Gly)$_n$ (Kluczyk et al., 2000, Peptides 21: 1411-1420), and (Glu-Lys)$_n$ (Klyczyk et al., 2000, supra), wherein n is 1 to 15.

- On page 26, replace the paragraph at lines 13-22 with the following replacement paragraph:

Linker sequences useful according to the invention serve to join monomers in the dimeric fluorescent polypeptides of the invention. A linker is preferably about 5 to about 50 amino acids in length, and more preferably about 10 to about 20 amino acids in length. An example of linkers useful in the invention are the Gly-Ala linkers taught by Huston et al., U.S. Patent No. 5,258,498, incorporated herein by reference. Additional useful linkers include, but are not limited to (Arg-Ala-Arg-Asp-Pro-Arg-Val-Pro-Val-Ala-Thr)$_{1-5}$ (SEQ ID NO: 8; Xu et al., 1999, Proc. Natl. Acad. Sci. U.S.A. 96: 151-156), (Gly-Ser)$_n$ (Shao et al., 2000, Bioconjug. Chem. 11: 822-826), (Thr-Ser-Pro)$_n$ (Kroon et al., 2000, Eur. J. Biochem. 267: 6740-6752), (Gly-Gly-Gly)$_n$ (Kluczyk et al., 2000, Peptides 21: 1411-1420), and (Glu-Lys)$_n$ (Klyczyk et al., 2000, supra), wherein n is 1 to 15 (each of the preceding references is also incorporated herein by reference).

- Replace Figure 4 with proposed amended Figure 4.

REMARKS

The amendments directed herein are made in order to add SEQ ID NOs corresponding to the SEQ ID NOs in the accompanying Sequence Listing.

The amendments include a proposed amendment to Figure 4, adding sequence identifiers SEQ ID NOs 5, 6 and 7 to the amino acid sequences depicted in the figure. In accord with 37 C.F.R. §1.121(d), a copy of Figure 4 is submitted showing proposed amendments to the drawing marked in red, along with a clean copy incorporating the proposed changes.

The amendments add no new matter.

Respectfully submitted,

Date: August 1, 2002

Name: Kathleen M. Williams
Registration No.: 34,380
Customer No.: 27495
Palmer & Dodge LLP
111 Huntington Avenue
Boston, MA 02199-7613
Tel: 617-239-0100

Version of Amendments Marked to Show Changes:

- On page 6, replace the paragraph at lines 8-15 with the following replacement paragraph:

--In one embodiment, the first polypeptide and the second polypeptide encoded by the polynucleotide are peptide bonded to each other via a linker sequence. In a preferred embodiment, the linker sequence encoded by the polynucleotide is from 5 to 50 amino acids long. In a further preferred embodiment, the linker sequence comprises one or more iterations of a peptide, for example the peptide RARDPRVPVAT (SEQ ID NO: 8; i.e., Arg-Ala-Arg-Asp-Pro-Arg-Val-Pro-Val-Ala-Thr). In a further preferred embodiment, the linker sequence is selected from the group consisting of $(Arg\text{-}Ala\text{-}Arg\text{-}Asp\text{-}Pro\text{-}Arg\text{-}Val\text{-}Pro\text{-}Val\text{-}Ala\text{-}Thr)_n$ (SEQ ID NO: 8), $(Gly\text{-}Ser)_n$, $(Thr\text{-}Ser\text{-}Pro)_n$, $(Gly\text{-}Gly\text{-}Gly)_n$, and $(Glu\text{-}Lys)_n$, wherein n is 1 to 15.--

- On page 15, replace the paragraph at lines 3-14 with the following replacement paragraph:

--As used herein, the term "linker sequence" refers to a sequence of peptide bonded amino acids that joins or links by peptide bonds two amino acid sequences or polypeptide domains that are not joined by peptide bonds in nature. A linker sequence is encoded in frame on a polynucleotide between the sequences encoding the two polypeptide domains joined by the linker. A linker is preferably 5 to 50 amino acids in length, more preferably 10 to 20 amino acids in length. An example of linkers useful in the invention are the Gly-Ala linkers taught by Huston et al., U.S. Patent No. 5,258,498, incorporated herein by reference. Additional useful linkers include, but are not limited to $(Arg\text{-}Ala\text{-}Arg\text{-}Asp\text{-}Pro\text{-}Arg\text{-}Val\text{-}Pro\text{-}Val\text{-}Ala\text{-}Thr)_{1\text{-}5}$ (SEQ ID NO: 8; Xu et al., 1999, Proc. Natl. Acad. Sci. U.S.A. 96: 151-156), $(Gly\text{-}Ser)_n$ (Shao et al., 2000, Bioconjug. Chem. 11: 822-826), $(Thr\text{-}Ser\text{-}Pro)_n$ (Kroon et al., 2000, Eur. J. Biochem. 267: 6740-6752), $(Gly\text{-}Gly\text{-}Gly)_n$ (Kluczyk et al., 2000, Peptides 21: 1411-1420), and $(Glu\text{-}Lys)_n$ (Klyczyk et al., 2000, supra), wherein n is 1 to 15.--

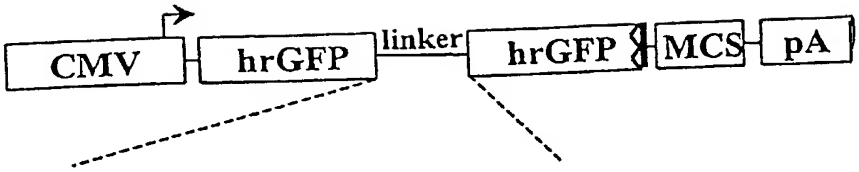
- On page 26, replace the paragraph at lines 13-22 with the following replacement paragraph:

--Linker sequences useful according to the invention serve to join monomers in the dimeric fluorescent polypeptides of the invention. A linker is preferably about 5 to about 50 amino acids in length, and more preferably about 10 to about 20 amino acids in length. An example of linkers useful in the invention are the Gly-Ala linkers taught by Huston et al., U.S. Patent No. 5,258,498, incorporated herein by reference. Additional useful linkers include, but

are not limited to (Arg-Ala-Arg-Asp-Pro-Arg-Val-Pro-Val-Ala-Thr)$_{1-5}$ (SEQ ID NO: 8; Xu et al., 1999, Proc. Natl. Acad. Sci. U.S.A. 96: 151-156), (Gly-Ser)$_n$ (Shao et al., 2000, Bioconjug. Chem. 11: 822-826), (Thr-Ser-Pro)$_n$ (Kroon et al., 2000, Eur. J. Biochem. 267: 6740-6752), (Gly-Gly-Gly)$_n$ (Kluczyk et al., 2000, Peptides 21: 1411-1420), and (Glu-Lys)$_n$ (Klyczyk et al., 2000, supra), wherein n is 1 to 15 (each of the preceding references is also incorporated herein by reference).--

- Replace Figure 4 with proposed amended Figure 4. The amendment adds SEQ ID NOs to the amino acid sequences depicted in the figure.

Figure 4

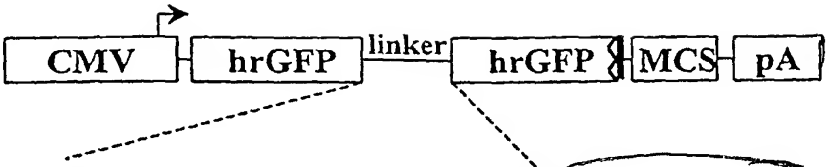


A. Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser (SEQ ID NO: 5)

B. Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser- Gly-Gly-Gly-Gly-Ser (SEQ ID NO: 6)

C. Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser (SEQ ID NO: 7)

Figure 4



A. Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser (SEQ ID NO: 5)

B. Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser- Gly-Gly-Gly-Gly-Ser (SEQ ID NO: 6)

C. Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser (SEQ ID NO: 7)